PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 02 April 2001 (02.04.01)	
International application No. PCT/US00/20040	**Applicant's or agent's file reference** MAR618/4006A
International filing date (day/month/year) 21 July 2000 (21.07.00)	**Priority date** (day/month/year) 22 July 1999 (22.07.99)
Applicant GAYED, Atef	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

20 February 2001 (20.02.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Zakaria EL KHODARY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PA NT COOPERATION TREAT

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 402 and 409)

To:

DAVIES, Tracey, B.
Vinson & Elkins L.L.P.
2300 First City Tower
1001 Fannin
Houston, TX 77002-6760
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 31 October 2000 (31.10.00)	
Applicant's or agent's file reference MAR618/4006A	**IMPORTANT NOTIFICATION**
International application No. PCT/US00/20040	International filing date (day/month/year) 21 July 2000 (21.07.00)
Applicant AVENTIS PHARMACEUTICALS, INC. et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. [X] **Correction of priority claim.** In accordance with the applicant's notice received on: 23 October 2000 (23.10.00), the following priority claim has been corrected to read as follows:

US 22 July 1999 (22.07.99) 60/228,815

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. [ ] **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. [ ] As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. [ ] **Priority claim considered not to have been made.**
   - [ ] The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
   - [ ] The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
   - [ ] The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

   The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(IB).

5. [ ] In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):

6. A copy of this notification has been sent to the receiving Office and
   - [X] to the International Searching Authority (where the international search report has not yet been issued).
   - [X] the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Mougamadou ABIDINE
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

Interna[illegible]pplication No
PCT/US 00/20040

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/18 A61K47/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 930 065 A (ETHICON INC) 21 July 1999 (1999-07-21) page 2, paragraph 6 page 2, paragraph 12 -page 3 page 7, paragraph 40; claims 1,4; example 5	1-44
A	US 3 489 837 A (HYMAN LEROY J) 13 January 1970 (1970-01-13) column 1, line 46 - line 57 column 2, line 52 - line 57	1-44
A	US 5 045 529 A (CHIANG CHING) 3 September 1991 (1991-09-03) column 3, line 31 - line 34 column 4, line 33 - line 42 column 7, line 3 - line 18 column 7, line 33 - line 35; claims 1,2,12	1-44

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 November 2000	10/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Marttin, E

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat[illegible]plication No
PCT/US 00/20040

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0930065 A	21-07-1999	US 5997893 A	07-12-1999
		AU 1317299 A	12-08-1999
		BR 9900318 A	16-05-2000
		CN 1228254 A	15-09-1999
		JP 11322559 A	24-11-1999
		PL 330952 A	02-08-1999
US 3489837 A	13-01-1970	NONE	
US 5045529 A	03-09-1991	AT 117805 T	15-02-1995
		CA 2049970 A	28-09-1990
		DE 69016415 D	09-03-1995
		DE 69016415 T	08-06-1995
		EP 0465510 A	15-01-1992
		JP 2938566 B	23-08-1999
		JP 4504306 T	30-07-1992
		WO 9011527 A	04-10-1990
		US 5558985 A	24-09-1996
		US 5320965 A	14-06-1994
		US 5304491 A	19-04-1994

1. Section I

The amended claims fulfill the requirements of Art 34(2)(b) PCT, in that they do not introduce subject-matter which was not present in the application as originally filed.

2. Section V

2.1 Cited Documents

The following documents (D) are referred to in this Opinion; the numbering will be adhered to in the rest of the procedure:

D1: EP 0 930 065 A (Ethicon Inc.) 21 July 1999

D2: US 3 489 837 (Hyman LeRoy J.) 13 January 1970

2.2 Art 33(2) PCT (Novelty)

The subject-matter of present claims 1-52 meets the requirements of Art 33(2) PCT.

None of the cited previous art documents discloses compositions comprising a pharmacologically active ingredient and, as antimicrobially active agents, benzethonium chloride and phenoxyethanol.

2.3 Art 33(3) PCT (Inventive step)

The subject-matter of present claims 1-52 does not meet the requirements of Art 33(3) PCT.

Document D1 discloses a topical composition (namely composition 17, cf. p. 7, ll. 53-56) containing phenoxyethanol (0.5%) and benzethonium chloride (0.08%), wherein the latter agent exerts an anti-microbial activity (cf. p. 2, last paragraph). Document D2 also discloses topical compositions comprising the aforementioned compounds (cf. passages cited in the Search Report) and cites the latter as a known antimicrobial agent. The addition to such compositions of a pharmaceutically active ingredient cannot be considered as inventive, the more so since the application as a whole does not show than any surprising or unexpected result is obtained.

3. Section VIII

3.1 The claims as a whole are not clear, since topical compositions are at first disclaimed in the independent claims and than claimed in the dependent ones (see claims 8, 9, 32, 36, 41 and 52.

3.2 The claims totally lack conciseness and are therefore unclear. Their dependency is in part unclear (cf. e.g. claim 8, which is a composition claim depending from a method claim which is 4 pages down in the set of claims), some of them are just duplicates of one another (cf. e.g. claims 33-36 and 48-50).

10/031922 US002
Rec'd PCT/PTO 22 JAN 2002

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising a pharmacologically active ingredient and an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth, and wherein the composition is not formulated for topical administration.

2. The composition of claim 1, further defined as comprising benzethonium chloride in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol in a concentration of from about 0.01 to about 2.0%.

3. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active ingredient is a cardiovascular agent.

4. The composition of claim 3, wherein said cardiovascular agent is diltiazem, digoxin, dopamine, digitalis, procainamide hydrochloride, lidocaine, verapomil, or levostatin.

5. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active ingredient is an agent for the treatment of the gastrointestinal system or liver.

6. The composition of claim 5, wherein said agent for the treatment of the gastrointestinal system or the liver is an antacid, a digestant or an emetic.

7. The composition of claim 5, wherein said agent for the treatment of the gastrointestinal system or the liver is lipase, furosamide, morphine, scopolamine, ranitidine.

8. The composition of claim 44, wherein said pharmacologically active ingredient is a topically active agent.

9. The composition of claim 8, wherein said topically active agent is bentonite, zinc oxide, dimethicone, or glycerin.

10. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is a hematologic agent.

11. The composition of claim 10, wherein said hematologic agent is heparin, streptokinase, urokinase, tissue plasminogen activator, or aspirin.

12. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is an antihistamine.

13. The composition of claim 12, wherein said antihistamine is theophylline, diphenhydramine, hydroxyzine or fexofenadine.

14. The composition of claim 12, wherein said antihistamine is fexofenadine.

15. The composition of claim 14, comprising about 0.005% benzethonium chloride, and about 0.25% phenoxyethanol.

16. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active ingredient is an antimicrobial.

17. The composition of claim 16, wherein said antimicrobial is penicillin, amoxycillin, kanamycin, neomycin, erythromycin, tetracycline, doxycycline, norfloxacin, or cyclosporin.

18. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is an antiepileptic or anti-seizure agent.

19. The composition of claim 18, wherein said antiepileptic or anti-seizure agent is phenytoin, dilantin, or phenobarbital.

20. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is a sedative or hypnotic.

21. The composition of claim 20, wherein said sedative or hypnotic is scopolomine, fexofenadine, or methaqualone.

22. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is a diuretic.

23. The composition of claim 22, wherein said diuretic is furosemide, amiloride, aminophylline, or theobromide.

24. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active ingredient is a psychopharmacologic agent.

25. The composition of claim 24, wherein said psychopharmacologic agent is an anti-psychotic or an antidepressant.

26. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active ingredient is an anti-migraine agent.

27. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is a hormone.

28. The composition of claims 1, 2, 45, 46 or 47, wherein said pharmacologically active agent is a protein or peptide.

29. The composition of claims 1, 2, 45, 46 or 47, further comprising a second active agent.

30. The composition of claim 29, wherein said second active agent is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a topically active agent, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

31. The composition of claims 1, 2, 45, 46 or 47, wherein said composition is a liquid, suspension, emulsion, solution, mixture, cream, inhalant, aerosol, gel, ointment, suppository, powder, tablet.

32. The composition of claims 1, 2, 45, 46 or 47, wherein said composition is administrable parenterally, via mucosa, topically, by suppository, by inhalation, orally, aurally, or ocularly.

33. A pharmaceutical carrier composition for use as a non-topically administered carrier of a pharmaceutically active ingredient, wherein said carrier comprises an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth in said composition.

34. The pharmaceutical carrier composition of claim 33, further defined as comprising benzethonium chloride in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol in a concentration of from about 0.01 to about 2.0%.

35. The pharmaceutical carrier composition of claims 33 or 34, wherein said pharmaceutically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a topically active agent, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

36. The pharmaceutical carrier composition of claims 48, 49 or 50, wherein said pharmaceutically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a topically active agent, a hematologic agent, an antihistamine, an

antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

37. A vial for containing multiple dosages of a pharmacologically active ingredient, wherein said vial contains a solution comprising said active ingredient and an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth in said composition, said solution formulated for administration by a route selected from the following: parenteral, muscosal, ocular, aural, oral, suppository, inhalation.

38. The vial of claim 37, further defined as comprising benzethonium chloride in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol in a concentration of from about 0.01 to about 2.0%.

39. The vial of claims 37 or 38, wherein said pharmacologically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

40. A pharmaceutical package for containing multiple dosages of a pharmacologically active ingredient, wherein said vial contains a solution comprising said active ingredient and an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth in said composition, the benzethonium chloride being present in a concentration of about 0.001% to about 0.005% and the phenoxyethanol being present in a concentration of about 0.01% to about 0.25% said solution formulated for administration by a route selected from the following: parenteral, muscosal, ocular, aural, oral, suppository, inhalation.

41. The pharmaceutical package of claim 40, wherein said pharmacologically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a

topically active agent, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

42. A method of inhibiting microbial growth in a non-topically-administrable solution comprising a pharmacologically active ingredient, said method comprising adding benzethonium chloride and phenoxyethanol to said solution.

43. The method of claim 42, wherein benzethonium chloride is added in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol is added in a concentration of from about 0.01 to about 2.0%.

44. The method of claims 42 or 43, wherein said pharmacologically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

45. A pharmaceutical composition comprising a pharmacologically active ingredient, an amount of benzethonium chloride and an amount of phenoxyethanol, wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth, and wherein the benzethonium chloride is present in a concentration of from about 0.001 to about 0.005%, and the phenoxyethanol is present in a concentration of from about 0.01 to about 0.25%.

46. A pharmaceutical composition comprising a pharmacologically active ingredient and an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth, and wherein the composition is formulated for administration by a route selected from the following: parenteral, mucosal, ocular, aural, oral, suppository, inhalation.

47. The pharmaceutical composition of claim 46, further defined as comprising benzethonium chloride in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol in a concentration of from about 0.01 to about 2.0%.

48. A pharmaceutical carrier composition for use as a carrier of a pharmaceutically active ingredient, wherein said carrier comprises an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth in said composition, and wherein the benzethonium chloride is present in a concentration of from about 0.001 to about 0.005%, and the phenoxyethanol is present in a concentration of from about 0.01 to about 0.25%.

49. A pharmaceutical carrier composition for use as a carrier of a pharmaceutically active ingredient, wherein said carrier comprises an amount of benzethonium chloride and an amount of phenoxyethanol wherein the amounts of benzethonium chloride and phenoxyethanol are effective to inhibit microbial growth in said composition, and wherein the carrier is formulated for administration by a route selected from the following: parenteral, mucosal, ocular, aural, oral, suppository, inhalation.

50. The pharmaceutical carrier composition of claim 33, further defined as comprising benzethonium chloride in a concentration of from about 0.001 to about 1.0%, and phenoxyethanol in a concentration of from about 0.01 to about 2.0%.

51. A method of inhibiting microbial growth in a solution comprising a pharmacologically active ingredient, said method comprising adding benzethonium chloride and phenoxyethanol to said solution, wherein the benzethonium chloride is added to be in a concentration of from about 0.001 to about 0.005%, and the phenoxyethanol is added to be in a concentration of from about 0.01 to about 0.25%.

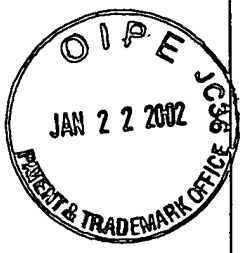
52. The method of claim 46, wherein said pharmacologically active ingredient is a cardiovascular agent, an agent for the treatment of gastrointestinal disorders, a topically active agent, a hematologic agent, an antihistamine, an antimicrobial, an antiepileptic, an anti-seizure

agent, a sedative, a hypnotic, a diuretic, a psychopharmacologic agent, an anti-migraine agent, a hormone, a protein or a peptide.

231741_1

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY



To:

PERRY, Robert Edward et al
GILL JENNINGS & EVERY
Broadgate House
7 Eldon Street
GB-EC2M 7LH London
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	13.12.2001
Applicant's or agent's file reference: REP06657EP	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/20040	21/07/2000	22/07/1999

Applicant
AVENTIS PHARMACEUTICALS, INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international applicatior

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of th report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation mus contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Senkel, H Tel.+49 89 2399-8071

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
REP06657EP		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/20040	21/07/2000	22/07/1999

International Patent Classification (IPC) or national classification and IPC
A61K47/18

Applicant
AVENTIS PHARMACEUTICALS, INC. et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
20/02/2001	13.12.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giacobbe, S Telephone No. +49 89 2399 8463

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20040

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, pages:

1-27	as originally filed

Claims, No.:

1-52	as received on	16/10/2001	with letter of	12/10/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have beer considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-52
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-52
Industrial applicability (IA)	Yes:	Claims	1-52
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
MAR618/4006A		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 20040	21/07/2000	22/07/1999
Applicant		
AVENTIS PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. --

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/20040

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K47/18 A61K47/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 930 065 A (ETHICON INC) 21 July 1999 (1999-07-21) page 2, paragraph 6 page 2, paragraph 12 -page 3 page 7, paragraph 40; claims 1,4; example 5	1-44
A	US 3 489 837 A (HYMAN LEROY J) 13 January 1970 (1970-01-13) column 1, line 46 - line 57 column 2, line 52 - line 57	1-44
A	US 5 045 529 A (CHIANG CHING) 3 September 1991 (1991-09-03) column 3, line 31 - line 34 column 4, line 33 - line 42 column 7, line 3 - line 18 column 7, line 33 - line 35; claims 1,2,12	1-44

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 November 2000	10/11/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Marttin, E

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/20040

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP 4504306 T	30-07-1992
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		US 5320965 A	14-06-1994
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